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NEWS 19	JUN 30	EMBASE, EMBAL, and LEMBASE updated with additional options to display authors and affiliated organizations
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NEWS 29	AUG 15	CAplus currency for Korean patents enhanced

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=> S (EVEC or fibulin-5 or DANCE) (8A) (integrin (4A) binding or bind or bound)
L1          20 (EVEC OR FIBULIN-5 OR DANCE) (8A) (INTEGRIN (4A) BINDING OR BIND
               OR BOUND)

=> S (EVEC or fibulin-5 or DANCE) (6A) (domain or motif or fragment or region or
section or portion or segment or part)
L2          96 (EVEC OR FIBULIN-5 OR DANCE) (6A) (DOMAIN OR MOTIF OR FRAGMENT
              OR REGION OR SECTION OR PORTION OR SEGMENT OR PART)

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PROCESSING COMPLETED FOR L3
L4 3 DUPLICATE REMOVE L3 (6 DUPLICATES REMOVED)

=> d l4 1-3 bib ab

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:1075903 CAPLUS
DN 143:344598
TI Cleavage of fibulin-5/DANCE by a serine protease is essential for elastogenesis in vivo: DANCE cleavage assay and drug screening
IN Nakamura, Tomoyuki; Hirai, Maretoshi
PA Kyoto University, Japan
SO PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005093057	A1	20051006	WO 2005-JP4274	20050304
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2561495	A1	20051006	CA 2005-2561495	20050304
	EP 1762610	A1	20070314	EP 2005-720545	20050304
	R: CH, DE, FR, GB, IT, LI				
	CN 1961073	A	20070509	CN 2005-80017559	20050304
	US 20070218003	A1	20070920	US 2006-594339	20060927
PRAI	JP 2004-96685	A	20040329		
	WO 2005-JP4274	W	20050304		

AB A method of screening that enables development of a medicine having a novel mechanism of action capable of regulating generation of an elastic fiber tissue; and various means that are requisite for the method; are provided. In particular, there are provided a polypeptide obtained by cleaving DANCE (developmental arteries and neural crest epidermal growth factor (EGF)-like) and a polynucleotide coding for the polypeptide; a method of cleaving DANCE; an antibody against the polypeptide obtained by cleaving DANCE; a method of measuring the amount of DANCE cleavage and a kit therefor; a DANCE variant and polynucleotide coding for the same; various DANCE complexes and a method of preparing the same; a method of screening a substance capable of regulating the activity of DANCE or a DANCE-specific protease, and a substance obtained by the screening method; an agent for regulating generation of an elastic fiber tissue; a kit comprising at least DANCE and a polynucleotide coding for the same; etc. Examples, etc. describe that DANCE is in vitro or in vivo cleaved by a serine protease, and that with respect to truncated DANCE, DANCE bind to each other and to LTBP2 (latent TGF-β-binding protein 2) and lysyl oxidase (LOX). It is presumed that (1) it no longer binds to cell surface integrin, (2) DANCE mols. no longer bind to each other and (3) the binding to LTBP2 is stronger than that to full-length DANCE (see Consideration 3), and that DANCE having an amino terminal domain cleaved exhibits substantially no activity of generating of elastic fibrous tissue (see Referential Example 2). Consequently, it is

proved that the amino terminal domain of DANCE is needed for generating of elastic fibrous tissue.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 3 MEDLINE on STN DUPLICATE 1
AN 2004591099 MEDLINE
DN PubMed ID: 15528465
TI Fibulin-5 is a novel binding protein for extracellular superoxide dismutase.
AU Nguyen Andrew D; Itoh Shinichi; Jeney Viktoria; Yanagisawa Hiromi; Fujimoto Mitsuaki; Ushio-Fukai Masuko; Fukai Tohru
CS Division of Cardiology, Department of Medicine, Emory University School of Medicine, Atlanta, Ga 30322, USA.
NC HL58000 (United States NHLBI)
R01 HL70187 (United States NHLBI)
SO Circulation research, (2004 Nov 26) Vol. 95, No. 11, pp. 1067-74. Electronic Publication: 2004-11-04.
Journal code: 0047103. E-ISSN: 1524-4571.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200506
ED Entered STN: 30 Nov 2004
Last Updated on STN: 16 Jun 2005
Entered Medline: 15 Jun 2005
AB The extracellular superoxide dismutase (ecSOD) plays an important role in atherosclerosis and endothelial function by modulating levels of the superoxide anion (O2*-) in the extracellular space. Although heparan sulfate proteoglycan is an important ligand for ecSOD, little is known about other biological binding partners of ecSOD. The goal of this study was to identify novel proteins that interact with ecSOD. A yeast two-hybrid screening of a human aorta cDNA library using ecSOD as bait identified fibulin-5 as a predominant binding protein for ecSOD. Further analysis showed that the binding domain of ecSOD within fibulin-5 mapped to its C-terminal domain. In vitro pulldown assays and coimmunoprecipitation analysis further confirmed that ecSOD interacts with fibulin-5 in vitro and in vivo. Studies using fibulin-5-/- mice indicated that fibulin-5 is required for binding of ecSOD to vascular tissue. Importantly, the decrease in tissue-bound ecSOD levels in aortas from fibulin-5-/- mice was associated with an increase in vascular O2*- levels. Furthermore, immunohistochemical analysis using ApoE-/- mice suggested a codistribution of ecSOD and fibulin-5 in atherosclerotic vessels. In summary, we provide in this study the first evidence that the ecSOD-fibulin-5 interaction is required for ecSOD binding to vascular tissues, thereby regulating vascular O2*- levels. This interaction may represent a novel mechanism for controlling vascular redox state in the extracellular space in various cardiovascular diseases such as atherosclerosis and hypertension in which oxidative stress is increased.

L4 ANSWER 3 OF 3 MEDLINE on STN DUPLICATE 2
AN 2002078083 MEDLINE
DN PubMed ID: 11805834
TI Fibulin-5 is an elastin-binding protein essential for elastic fibre development in vivo.
AU Yanagisawa Hiromi; Davis Elaine C; Starcher Barry C; Ouchi Takashi;

Yanagisawa Masashi; Richardson James A; Olson Eric N
CS Department of Molecular Biology, University of Texas Southwestern Medical Center at Dallas, Texas 75390, USA.. hyanagisawa@aol.com
SO Nature, (2002 Jan 10) Vol. 415, No. 6868, pp. 168-71.
Journal code: 0410462. ISSN: 0028-0836.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200202
ED Entered STN: 28 Jan 2002
Last Updated on STN: 15 Feb 2002
Entered Medline: 14 Feb 2002
AB Extracellular elastic fibres provide mechanical elasticity to tissues and contribute towards the processes of organ remodelling by affecting cell-cell signalling. The formation of elastic fibres requires the assembly and crosslinking of tropoelastin monomers, and organization of the resulting insoluble elastin matrix into functional fibres. The molecules and mechanisms involved in this process are unknown. Fibulin-5 (also known as EVEC/DANCE) is an extracellular matrix protein abundantly expressed in great vessels and cardiac valves during embryogenesis, and in many adult tissues including the aorta, lung, uterus and skin, all of which contain abundant elastic fibres. Here we show that fibulin-5 is a calcium-dependent, elastin-binding protein that localizes to the surface of elastic fibres in vivo. fibulin-5-/- mice develop marked elastinopathy owing to the disorganization of elastic fibres, with resulting loose skin, vascular abnormalities and emphysematous lung. This phenotype, which resembles the cutis laxa syndrome in humans, reveals a critical function for fibulin-5 as a scaffold protein that organizes and links elastic fibres to cells. This function may be mediated by the RGD motif in fibulin-5, which binds to cell surface integrins, and the Ca2+-binding epidermal growth factor (EGF) repeats, which bind elastin.

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PROCESSING COMPLETED FOR L1
L6            7 DUPLICATE REMOVE L1 (13 DUPLICATES REMOVED)

=> d l6 1-7 bib ab

L6   ANSWER 1 OF 7     MEDLINE on STN                    DUPLICATE 1
AN   2007035536     MEDLINE
DN   PubMed ID: 17130242
TI   Molecular analysis of fibulin-5 function during de novo synthesis of
     elastic fibers.
AU   Zheng Qian; Davis Elaine C; Richardson James A; Starcher Barry C; Li
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Tiansen; Gerard Robert D; Yanagisawa Hiromi
CS Department of Molecular Biology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., Dallas, TX 75390-9148, USA.
NC HL 071157 (United States NHLBI)
SO Molecular and cellular biology, (2007 Feb) Vol. 27, No. 3, pp. 1083-95. Electronic Publication: 2006-11-27. Journal code: 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, N.I.H., EXTRAMURAL) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200703
ED Entered STN: 20 Jan 2007 Last Updated on STN: 6 Mar 2007 Entered Medline: 5 Mar 2007
AB Elastic fibers contribute to the structural support of tissues and to the regulation of cellular behavior. Mice deficient for the fibulin-5 gene (fbln5(-/-)) were used to further elucidate the molecular mechanism of elastic fiber assembly. Major elastic fiber components were present in the skin of fbln5(-/-) mice despite a dramatic reduction of mature elastic fibers. We found that fibulin-5 preferentially bound the monomeric form of elastin through N-terminal and C-terminal elastin-binding regions and to a preexisting matrix scaffold through calcium-binding epidermal growth factor (EGF)-like (CB-EGF) domains. We further showed that adenovirus-mediated gene transfer of fbln5 was sufficient to regenerate elastic fibers and increase elastic fiber-cell connections in vivo. A mutant fibulin-5 lacking the first 28 amino acids of the first CB-EGF domain, however, was unable to rescue elastic fiber defects. Fibulin-5 thus serves as an adaptor molecule between monomeric elastin and the matrix scaffold to aid in elastic fiber assembly. These results also support the potential use of fibulin-5 as a therapeutic agent for the treatment of elastinopathies.

L6 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:223863 CAPLUS
TI Construction of Electrocatalytic Electrodes Bearing the Triphenylamine Nucleus Covalently Bound to Carbon. A Halogen Dance in Protonated Aminotriphenylamines
AU Mayers, Brian T.; Fry, Albert J.
SO Organic Letters (2006), 8(6), 1253 CODEN: ORLEF7; ISSN: 1523-7060
PB American Chemical Society
DT Journal; Errata
LA English
AB Unavailable

L6 ANSWER 3 OF 7 MEDLINE on STN DUPLICATE 2
AN 2006051293 MEDLINE
DN PubMed ID: 16435847
TI Construction of electrocatalytic electrodes bearing the triphenylamine nucleus covalently bound to carbon. A halogen dance in protonated aminotriphenylamines.
AU Mayers Brian T; Fry Albert J
CS Chemistry Department, Wesleyan University, Middletown, Connecticut 06459, USA.
SO Organic letters, (2006 Feb 2) Vol. 8, No. 3, pp. 411-4. Journal code: 100890393. ISSN: 1523-7060.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS NONMEDLINE; PUBMED-NOT-MEDLINE
EM 200610
ED Entered STN: 27 Jan 2006
Last Updated on STN: 19 Oct 2006
Entered Medline: 18 Oct 2006
AB [reaction: see text]. The triarylamine nucleus has been attached to a carbon fiber electrode by diazotization of an aminotriphenylamine followed by electrochemical reduction. The resulting electrodes can electrocatalyze the oxidation of organic substrates. In acid, 4-amino-4',4' '-dibromotriphenylamine undergoes dismutation into a mixture of amines containing from 0 to 3 bromine atoms.

L6 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:1075903 CAPLUS
DN 143:344598
TI Cleavage of fibulin-5/DANCE by a serine protease is essential for elastogenesis in vivo: DANCE cleavage assay and drug screening
IN Nakamura, Tomoyuki; Hirai, Maretoshi
PA Kyoto University, Japan
SO PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005093057	A1	20051006	WO 2005-JP4274	20050304
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2561495	A1	20051006	CA 2005-2561495	20050304
	EP 1762610	A1	20070314	EP 2005-720545	20050304
	R: CH, DE, FR, GB, IT, LI				
	CN 1961073	A	20070509	CN 2005-80017559	20050304
	US 20070218003	A1	20070920	US 2006-594339	20060927
PRAI	JP 2004-96685	A	20040329		
	WO 2005-JP4274	W	20050304		

AB A method of screening that enables development of a medicine having a novel mechanism of action capable of regulating generation of an elastic fiber tissue; and various means that are requisite for the method; are provided. In particular, there are provided a polypeptide obtained by cleaving DANCE (developmental arteries and neural crest epidermal growth factor (EGF)-like) and a polynucleotide coding for the polypeptide; a method of cleaving DANCE; an antibody against the polypeptide obtained by cleaving DANCE; a method of measuring the amount of DANCE cleavage and a kit therefor; a DANCE variant and polynucleotide coding for the same; various DANCE complexes and a method of preparing the same; a method of screening a substance capable of regulating the activity of DANCE or a DANCE-specific protease, and a substance obtained by the screening method; an agent for regulating generation of an elastic fiber tissue; a kit comprising at least DANCE and a polynucleotide coding for the same; etc. Examples, etc. describe that DANCE is in vitro or in vivo cleaved by a serine protease,

and that with respect to truncated DANCE, DANCE bind to each other and to LTBP2 (latent TGF-β-binding protein 2) and lysyl oxidase (LOX). It is presumed that (1) it no longer binds to cell surface integrin, (2) DANCE mols. no longer bind to each other and (3) the binding to LTBP2 is stronger than that to full-length DANCE (see Consideration 3), and that DANCE having an amino terminal domain cleaved exhibits substantially no activity of generating of elastic fibrous tissue (see Referential Example 2). Consequently, it is proved that the amino terminal domain of DANCE is needed for generating of elastic fibrous tissue.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 7 MEDLINE on STN DUPLICATE 3
AN 2004591099 MEDLINE
DN PubMed ID: 15528465
TI Fibulin-5 is a novel binding protein for extracellular superoxide dismutase.
AU Nguyen Andrew D; Itoh Shinichi; Jeney Viktoria; Yanagisawa Hiromi; Fujimoto Mitsuaki; Ushio-Fukai Masuko; Fukai Tohru
CS Division of Cardiology, Department of Medicine, Emory University School of Medicine, Atlanta, Ga 30322, USA.
NC HL58000 (United States NHLBI)
R01 HL70187 (United States NHLBI)
SO Circulation research, (2004 Nov 26) Vol. 95, No. 11, pp. 1067-74.
Electronic Publication: 2004-11-04.
Journal code: 0047103. E-ISSN: 1524-4571.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200506
ED Entered STN: 30 Nov 2004
Last Updated on STN: 16 Jun 2005
Entered Medline: 15 Jun 2005
AB The extracellular superoxide dismutase (ecSOD) plays an important role in atherosclerosis and endothelial function by modulating levels of the superoxide anion (O2*-) in the extracellular space. Although heparan sulfate proteoglycan is an important ligand for ecSOD, little is known about other biological binding partners of ecSOD. The goal of this study was to identify novel proteins that interact with ecSOD. A yeast two-hybrid screening of a human aorta cDNA library using ecSOD as bait identified fibulin-5 as a predominant binding protein for ecSOD. Further analysis showed that the binding domain of ecSOD within fibulin-5 mapped to its C-terminal domain. In vitro pulldown assays and coimmunoprecipitation analysis further confirmed that ecSOD interacts with fibulin-5 in vitro and in vivo. Studies using fibulin-5-/- mice indicated that fibulin-5 is required for binding of ecSOD to vascular tissue. Importantly, the decrease in tissue-bound ecSOD levels in aortas from fibulin-5-/- mice was associated with an increase in vascular O2*- levels. Furthermore, immunohistochemical analysis using ApoE-/- mice suggested a codistribution of ecSOD and fibulin-5 in atherosclerotic vessels. In summary, we provide in this study the first evidence that the ecSOD-fibulin-5 interaction is required for ecSOD binding to vascular tissues, thereby regulating vascular O2*- levels. This interaction may represent a novel mechanism for controlling vascular redox state in the extracellular space in various cardiovascular diseases such as atherosclerosis and hypertension in which oxidative stress is

increased.

L6 ANSWER 6 OF 7 MEDLINE on STN DUPLICATE 4
AN 2004329556 MEDLINE
DN PubMed ID: 15231070
TI Fibulin-5 antagonizes vascular endothelial growth factor (VEGF) signaling and angiogenic sprouting by endothelial cells.
AU Albig Allan R; Schiemann William P
CS Program in Cell Biology, Department of Pediatrics, National Jewish Medical and Research Center, Denver, Colorado, USA.
NC CA095519 (United States NCI)
CA99321 (United States NCI)
SO DNA and cell biology, (2004 Jun) Vol. 23, No. 6, pp. 367-79.
Journal code: 9004522. ISSN: 1044-5498.
CY United States
DT (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200408
ED Entered STN: 3 Jul 2004
Last Updated on STN: 4 Aug 2004
Entered Medline: 3 Aug 2004
AB Fibulin-5 (FBLN-5) is a widely expressed, integrin-binding extracellular matrix protein that mediates endothelial cell adhesion and scaffolds cells to elastic fibers. It is also a gene target of TGF-beta in fibroblasts and endothelial cells that regulates cell proliferation and motility in a context-specific manner. Whereas FBLN-5 expression is low in adult vasculature, its expression is high in developing and injured vasculature, implicating FBLN-5 in regulating angiogenesis and endothelial cell function. We show here that TGF-beta stimulates FBLN-5 expression in endothelial cells, and that this response was inhibited by coadministration of the proangiogenic factor, VEGF. FBLN-5 expression was downregulated significantly during endothelial cell tubulogenesis, implying that FBLN-5 expression antagonizes angiogenesis. Accordingly, FBLN-5 overexpression in or recombinant FBLN-5 treatment of endothelial cells abrogated their ability to undergo angiogenic sprouting, doing so by inhibiting endothelial cell proliferation and invasion through Matrigel matrices. Moreover, FBLN-5 antagonized VEGF signaling in endothelial cells, as well as enhanced their expression of the antiangiogenic factor, thrombospondin-1. Finally, the ability of FBLN-5 to antagonize angiogenic processes was determined to be independent of its integrin-binding RGD motif. Collectively, our findings establish FBLN-5 as a novel antagonist of angiogenesis and endothelial cell activities, and offer new insights into why tumorigenesis downregulates FBLN-5 expression.

L6 ANSWER 7 OF 7 MEDLINE on STN DUPLICATE 5
AN 2002400945 MEDLINE
DN PubMed ID: 12021267
TI Context-specific effects of fibulin-5 (DANCE/EVEC) on cell proliferation, motility, and invasion. Fibulin-5 is induced by transforming growth factor-beta and affects protein kinase cascades.
AU Schiemann William P; Blobe Gerard C; Kalume Dario E; Pandey Akhilesh; Lodish Harvey F
CS Whitehead Institute for Biomedical Research, Cambridge, MA 02142, USA.. schiemannwp@njc.org
NC CA 63260 (United States NCI)
SO The Journal of biological chemistry, (2002 Jul 26) Vol. 277, No. 30, pp.

27367-77. Electronic Publication: 2002-05-20.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200208
ED Entered STN: 2 Aug 2002
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AB Fibulin-5 (FBLN-5; also known as DANCE or EVEC) is an integrin-binding extracellular matrix protein that mediates endothelial cell adhesion; it is also a calcium-dependent elastin-binding protein that scaffolds cells to elastic fibers, thereby preventing elastinopathy in the skin, lung, and vasculature. Transforming growth factor-beta (TGF-beta) regulates the production of cytokines, growth factors, and extracellular matrix proteins by a variety of cell types and tissues. We show here that TGF-beta stimulates murine 3T3-L1 fibroblasts to synthesize FBLN-5 transcript and protein through a Smad3-independent pathway. Overexpression of FBLN-5 in 3T3-L1 cells increased DNA synthesis and enhanced basal and TGF-beta-stimulated activation of ERK1/ERK2 and p38 mitogen-activated protein kinase (MAPK). FBLN-5 overexpression also augmented the tumorigenicity of human HT1080 fibrosarcoma cells by increasing their DNA synthesis, migration toward fibronectin, and invasion through synthetic basement membranes. In stark contrast, FBLN-5 expression was down-regulated in the majority of metastatic human malignancies, particularly in cancers of the kidney, breast, ovary, and colon. Unlike its proliferative response in fibroblasts, FBLN-5 overexpression in mink lung Mv1Lu epithelial cells resulted in an antiproliferative response, reducing their DNA synthesis and cyclin A expression. Moreover, FBLN-5 synergizes with TGF-beta in stimulating AP-1 activity in Mv1Lu cells, an effect that was abrogated by overexpression of dominant-negative versions of either MKK1 or p38 MAPKalpha. Accordingly, both the stimulation and duration of ERK1/ERK2 and p38 MAPK by TGF-beta was enhanced in Mv1Lu cells expressing FBLN-5. Our findings identify FBLN-5 as a novel TGF-beta-inducible target gene that regulates cell growth and motility in a context-specific manner and affects protein kinase activation by TGF-beta. Our findings also indicate that aberrant FBLN-5 expression likely contributes to tumor development in humans.